We Claim:

1. A method of generating a genetic reference dataset for use in the determination of the predicted probability for an individual of having a susceptibility for a developmental disorder due to genetic factors or for developing a developmental disorder due to genetic factors or for having offspring that develop a developmental disorder due to genetic factors comprising:

(a) collecting a biological sample from a human subject; wherein the human subject is selected from the group consisting of a diagnostic proband, a blood relative of the diagnostic proband, an affected proband, a blood relative of the affected proband, a control proband, and a blood relative of the control proband; wherein the biological sample contains nucleic acids and/or proteins from the human subject;

(b) analyzing the nucleic acids and/or proteins from the biological sample; wherein said analyzing results in a partial or full genotype for the alleles of the genes involved in folate, pyridoxine, and/or cobalamin metabolism; wherein said partial or full genotype forms a dataset of genetic explanatory variables for the human subject; and

(c) compiling the dataset of genetic explanatory variables from multiple human subjects into a genetic reference dataset.

2. A method of generating a genetic and environmental reference dataset for use in the determination of the predicted probability for an individual of having a susceptibility for a developmental disorder due to genetic factors and environmental factors or for developing a developmental disorder due to genetic factors and environmental factors or for having offspring that develop a developmental disorder due to genetic factors and environmental factors comprising:

(a) obtaining dietary and epidemiological information for environmental explanatory variables for the human subjects of Claim 1; and

(b) combining said environmental explanatory variables with a genetic reference dataset for the human subjects.

3. The method of Claim 2 wherein the developmental disorder is selected from the group consisting of schizophrenia, spina bifida cystica, Tourette's syndrome, dyslexia, conduct disorder, attention-deficit hyperactivity disorder, bipolar illness, autism, chronic multiple tic syndrome and obsessive-compulsive disorder.

4. A method of generating an environmental reference dataset for use in the determination of the predicted probability for an individual of having a susceptibility for a developmental disorder due to environmental factors or for developing a developmental disorder due to environmental factors or for having offspring that develop a developmental disorder due to environmental factors comprising:

(a) obtaining dietary and epidemiological information for environmental explanatory variables for a human subject; wherein the human subject is selected from the group consisting of a diagnostic proband, a blood relative of the diagnostic proband, an affected proband, a blood relative of the affected proband, a control proband, and a blood relative of the control proband; and

(b) compiling a dataset of environmental explanatory variables from multiple human subjects into an environmental reference dataset for the human subjects.

5. A method of estimating the genetic susceptibility of an individual to have or to develop a developmental disorder comprising:

(a) collecting a biological sample from one or more participants; wherein a participant is either the individual or a blood relative of the individual; and wherein the biological sample contains nucleic acids and/or proteins of the participant;

(b) analyzing the nucleic acids and/or proteins from the biological sample; wherein said analyzing results in a partial or full genotype for the alleles of the genes

involved in folate, pyridoxine, and/or cobalamin metabolism; and wherein said partial or full genotype forms a dataset of genetic explanatory variables for the participants;

(c) adding the datasets of genetic explanatory variables obtained from steps (a) and (b) to a genetic reference dataset therein forming a combined genetic dataset;

(d) formulating a model comprising the genetic explanatory variables obtained from the participants; and

(e) analyzing the combined genetic dataset; wherein a predicted probability for the individual of having or developing a developmental disorder is determined; and wherein the genetic susceptibility of an individual to have or to develop a developmental disorder is estimated.

6. The method of Claim 5 wherein said analyzing the combined genetic dataset is performed by binary linear regression.

7. The method of Claim 6 further comprising the step of :

(f) modifying the model by adding or subtracting a genetic explanatory variable; and re-analyzing the combined genetic dataset by binary logistic regression; wherein a model is chosen that best fits the data.

8. The method of Claim 7 further comprising the step of :

(g) testing the model for goodness of fit.

9. The method of Claim 8 wherein the binary linear regression is performed with the SAS system.

10. The method of Claim 5 wherein the developmental disorder is selected from the group consisting of schizophrenia, spina bifida cystica, Tourette's syndrome, dyslexia, conduct disorder, attention-deficit hyperactivity disorder, bipolar illness, autism, chronic multiple tic syndrome and obsessive-compulsive disorder.

11. The method of Claim 10 wherein the developmental disorder is schizophrenia and the individual is suspected of being genetically susceptible of having or for developing schizophrenia.

12. The method of Claim 11 wherein the individual is suspected of being genetically susceptible for having or for developing schizophrenia because a blood relative has schizophrenia.

13. The method of Claim 12 wherein the blood relative is a parent, a sibling, or a grandparent.

14. The method of Claim 13 wherein the blood relative is a parent and wherein the parent is the mother of the individual.

15. A method of estimating the genetic and environmental susceptibility of an individual to have or to develop a developmental disorder comprising:

(a) collecting a biological sample from one or more participants; wherein a participant is either the individual or a blood relative of the individual; and wherein the biological sample contains nucleic acids and/or proteins of the participant;

(b) analyzing the nucleic acids and/or proteins from the biological sample; wherein said analyzing results in a partial or full genotype for the alleles of the genes involved in folate, pyridoxine, and/or cobalamin metabolism; and wherein said partial or full genotype forms a dataset of genetic explanatory variables for the participants;

(c) obtaining dietary and epidemiological information for environmental explanatory variables for the participants; wherein said information forms a dataset of environmental explanatory variables for the participants;

(d) adding the datasets of genetic explanatory variables obtained from steps (a) and (b) and the dataset of environmental explanatory variables of step (c) to a genetic and environmental reference dataset therein forming a combined genetic and environmental dataset;

(e) formulating a model comprising the genetic and environmental explanatory variables obtained from the participants; and

(f) analyzing the combined genetic and environmental dataset by binary logistic regression;

wherein a predicted probability for the individual of having or developing a developmental disorder is determined; and wherein the genetic and environmental susceptibility of an individual to have or to develop a developmental disorder is estimated.

16. The method of Claim 15 further comprising the step of :

(g) modifying the model by adding or subtracting a genetic or environmental explanatory variable; and re-analyzing the combined genetic and environmental dataset by binary logistic regression; wherein a model is chosen that best fits the data.

17. The method of Claim 16 further comprising the step of :

(h) testing the model for goodness of fit.

18. The method of Claim 17 wherein the binary linear regression is performed with the SAS system.

19. A method of estimating the susceptibility of an individual to have offspring that develop a developmental disorder comprising:

(a) collecting a biological sample from one or more participants; wherein a participant is either the individual or a blood relative of the individual; and wherein the biological sample contains nucleic acids and/or proteins of the participant;

(b) analyzing the nucleic acids and/or proteins from the biological sample; wherein said analyzing results in a partial or full genotype for the alleles of the genes involved in folate, pyridoxine, and/or cobalamin metabolism; and wherein said partial or full genotype forms a dataset of genetic explanatory variables for the participants;

(c) adding the datasets of genetic explanatory variables obtained from steps (a) and (b) to a genetic reference dataset therein forming a combined genetic dataset;

(d) formulating a model comprising the genetic explanatory variables obtained from the participants; and

(e) analyzing the combined genetic dataset by binary logistic regression;

wherein a predicted probability for the individual to have offspring that develop a developmental disorder is determined; and wherein the genetic and environmental susceptibility of an individual to have offspring that develop a developmental disorder is estimated.

20. The method of Claim 19 further comprising the step of :

(f) modifying the model by adding or subtracting a genetic explanatory variable; and re-analyzing the combined genetic dataset by binary logistic regression; wherein a model is chosen that best fits the data.

21. The method of Claim 20 further comprising the step of :

(g) testing the model for goodness of fit.

22. The method of Claim 21 wherein the binary linear regression is performed with the SAS system.

23. The method of Claim 22 wherein the individual is a pregnant woman.

24. A method of lowering the risk of a pregnant woman who has been determined by the method of Claim 23 to be susceptible to have offspring that develop a developmental disorder comprising administering methylfolate, cobalamin or pyridoxine to the pregnant woman, wherein said administering lowers the risk of the pregnant woman of giving birth to offspring with a developmental disorder.

25. A method of determining if any treatment is advisable for a pregnant woman who has been determined by the method of Claim 23 to be susceptible to having offspring that develop a developmental disorder comprising determining the

concentration of a risk factor from a tissue sample or body fluid from the pregnant woman; wherein when the concentration of the risk factor is statistically above or below an accepted normal range, treatment is advisable.

26. A method of monitoring the effect of the administration of methylfolate, cobalamin or pyridoxine to the pregnant woman of Claim 25, comprising determining the concentration of a risk factor from a tissue sample or body fluid from the pregnant woman; and wherein when the concentration of the risk factor is statistically within an accepted normal range, the treatment is effective.

27. The method of Claim 26 wherein the risk factor is selected from the group consisting of homocysteine, folate, and cobalamin.

28. The method of Claim 22 wherein the individual is the mate of a pregnant woman.

29. A method of treating an asymptomatic individual determined by the method of Claim 23 to be susceptible for developing a developmental disorder comprising administering methylfolate, cobalamin or pyridoxine.

30. An isolated nucleic acid encoding a genetic variant of human dihydrofolate reductase comprising a nucleotide sequence having a 19 base-pair deletion spanning nucleotides 540 to 558 of the nucleotide sequence of SEQ ID NO:41.

31. The isolated nucleic acid of Claim 30 that has the nucleotide sequence of SEQ ID NO:42.

32. An expression vector comprising the nucleic acid of Claim 30 operably associated with an expression control sequence, wherein the nucleic acid is selected from the group consisting of cDNA or genomic DNA.

33. A PCR primer that can be used to distinguish SEQ ID NO:42 from the nucleotide sequence selected from the group consisting of SEQ ID NO:41 and SEQ ID NO:45.

34. The PCR primer of Claim 33 that comprises 10 to 50 consecutive nucleotides from the nucleotide sequence selected from the group of SEQ ID NO: 41, the complementary strand of SEQ ID NO: 41, SEQ ID NO:42, the complementary strand of SEQ ID NO: 42, SEQ ID NO:45, and the complementary strand of SEQ ID NO: 45.

35. The PCR primer of Claim 34 wherein the 10 to 50 consecutive nucleotides are from nucleotides 350 to 530 of SEQ ID NO:41.

36. The PCR primer of Claim 35 having the nucleotide sequence of 5'-CTA AAC TGC ATC GTC GCT GTG-3' (SEQ ID NO:38).

37. The PCR primer of Claim 36 wherein the 10 to 50 consecutive nucleotides are from the complementary strand of nucleotides 550 to 850 of SEQ ID NO:41.

38. The PCR primer of Claim 37 having the nucleotide sequence of 5'-AAA AGG GGA ATC CAG TCG G-3' (SEQ ID NO:39).

39. An isolated nucleic acid that hybridizes under standard hybridization conditions to a nucleic acid having the nucleotide sequence ACCTGGGCGGGACGCGCCA (SEQ ID NO:40) or a sequence complementary to SEQ ID NO:40; wherein said isolated nucleic acid consists of 12 to 48 nucleotides.

40. An isolated nucleic acid that hybridizes to the nucleotide sequence of SEQ ID NO:42, but not to the nucleotide sequence of SEQ ID NO:41; when said hybridizing is performed under identical conditions.

41. An isolated nucleic acid that hybridizes to the complementary strand of the nucleotide sequence of SEQ ID NO:42, but not to the complementary strand of the nucleotide sequence of SEQ ID NO:41; when said hybridizing is performed under identical conditions.

42. An isolated nucleic acid that hybridizes to the nucleotide sequence of SEQ ID NO:41, but not to the nucleotide sequence of SEQ ID NO:42; when said hybridizing is performed under identical conditions.

43. An isolated nucleic acid that hybridizes to the complementary strand of the nucleotide sequence of SEQ ID NO:41, but not to the complementary strand of the nucleotide sequence of SEQ ID NO:42; when said hybridizing is performed under identical conditions.

44. The method of Claim 5 wherein said analyzing the nucleic acids and/or proteins from the biological sample comprises determining if the biological sample contains a genetic variant of human dihydrofolate reductase having a nucleotide sequence with a 19 base-pair deletion spanning nucleotides 540 to 558 of the nucleotide sequence of SEQ ID NO:41; and wherein the genetic variant of human dihydrofolate reductase is an explanatory variable.

45. The method of Claim 44 wherein said determining is performed by a method selected from the group consisting of PCR, special PCR, RT PCR, RFLP analysis, SSCP, and FISH.

46. The method of Claim 1 wherein said analyzing the nucleic acids and/or proteins from the biological sample comprises determining if the biological sample contains the genetic variant of human dihydrofolate reductase having a nucleotide sequence with a 19 base-pair deletion spanning nucleotides 540 to 558 of the nucleotide sequence of SEQ ID NO:41; and wherein the genetic variant of human dihydrofolate reductase is an explanatory variable.

47. The method of Claim 46 wherein said determining is performed by a method selected from the group consisting of PCR, special PCR, RT PCR, RFLP analysis, SSCP, and FISH.